REMARKS/ARGUMENTS

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of two months of the period for response to the Office Action. Authorization to charge the prescribed fee to our deposit account is enclosed.

The Examiner retained rejections:

1. Claims 19, 22, 25 and 27 to 28 are rejected under 35 USC 102(e) as being anticipated by Gurtiss III (USP 5,389,368).

2. Claims 20 to 21, 24 and 26 are rejected under 35 USC 103(a) as being unpatentable over Gurtiss III in view of Brunham (WO 98/02546).

Reconsideration is requested having regard to the revisions made to claim 19 and the arguments presented herein. It is noted that claim 19 has been amended to refer to the term "in cells of a host" to "by cells of a host" and the term "in said attenuated bacterial" by "by said attenuated bacteria". These changes are to emphasize the distinctions over the prior art. In addition, claim 19 has been amended to refer to an auxotrophic bacteria, consistent with the Examiner's amendment in related application No. 10/699,882. Basis for this change can be found, for example on page 8, line 12.

Claim 19 is directed to an attenuated strain of an auxotrophic bacterium harbouring a vector comprising a nucleic acid encoding at least one immunoprotection inducing *Chlamydia* protein or a fragment thereof which generates a *Chlamydia* protein specific immune response and a promoter operatively coupled to the nucleic acid molecules for expression of the *Chlamydia* protein or fragment thereof by cells of a host to which the strain is administered but not by the attenuated bacteria.

The attenuated bacteria herein are distinguished from the prior art in requiring that the promoter directs expression of the *Chlamydia* protein or fragment by cells of a host to which the attenuated strain is administered but not by the attenuated bacteria itself.

As described in the specification, for example, on page 8, lines 7 to 15, the expression of the DNA is effected when the bacterial vector has released the DNA into the appropriate host cells, such as macrophage or dendritic cells. After uptake of the bacterial vector by the cells, the auxotrophic bacteria dies and the plasmid DNA then is released into the cytoplasm of the infected host cells and the encoded gene expressed in the host cells.

Gurtiss III provides a vaccine for immunization of a vertebrate or invertebrate comprising an avirulent derivative of a microbe. The derivative is substantially incapable of producing functional adenylate cyclase and cyclic AMP receptor protein while being capable of expressing a recombinant gene derived from a pathogen of the vertebrate or invertebrate to produce an antigen capable of inducing an immune response in the vertebrate or invertebrate against the pathogen (col. 3, ll. 42 to 50). Gurtiss III also disclose a method of stimulating the immune system of a vertebrate or invertebrate by administering the vaccine to the vertebrate or invertebrate (col. 3, line 60 to col. line 2).

Gurtiss III also describes a carrier microbe for the synthesis of a vertebrate or invertebrate host protein comprising the avirulent derivative of a pathogenic microbe which is capable of expressing a recombinant gene derived from a vertebrate or invertebrate host to produce a product capable of suppressing, modulating or augmenting an immune response to the vertebrate or invertebrate (col. 4, ll. 3 to 12).

It is clear from these passages that, in Gurtiss III, the avirulent microbe directs expression of the foreign antigen in the avirulent microbe. There is no

disclosure in Gurtiss III of an avirulent microbe in which the foreign antigen is expressed by the host and not by the microbe, as required by applicants claims.

Thus, there is a fundamental difference between the attenuated bacteria defined in applicants claims and the cited prior art. In the present invention, the attenuated bacteria is employed as a carrier for the vector and it is the promoter in the DNA construct which directs expression of the *Chlamydia* protein or fragment thereof by the host cells only upon administration thereto and not by the attenuated bacteria, quite the reverse of Gurtiss III.

It is agreed with the Examiner that the avirulent microbes preferably are derived from *Salmonella* (col. 6, ll. 12 to 15) and that *Chlamydia* is identified as a pathogenic microorganism useful in Gurtiss III constructs (claim 6 and also in col. 6, ll. 52 to 53). However, Gurtiss III states, in col. 6, ll. 16 to 34:

> "In another embodiment of the invention, the avirulent derivative of a pathogenic microbe also referred to herein as a carrier bacteria can be used to deliver selected antigens to the GALT ..... If these carrier bacteria contain and express a recombinant gene from a pathogenic organism, antibodies against the antigenic gene product produced from the pathogen will be induced. With the advent of recombinant DNA techniques, it now becomes possible to develop totally unique vaccines in which specific antigens are produced, not by the etiologic agent, but by another host strain of bacteria capable of expressing the gene for that antigen." (Emphasis added).

It is absolutely clear from this passage that Gurtiss III is contemplating expression of the foreign gene by the avirulent bacteria. In addition, Gurtiss III defines the term "expression of a gene" as:

> "Expression of a gene means that the information inherent in the structure of the gene is transformed into a physical product ... by the biochemical mechanisms of the cell. in which the gene is located." (Emphasis added) (col. 9, ll. 37 to 43)

The patentee elaborates on the use of the avirulent microbe as a carrier (in col. 10, ll. 10 to 24):

> ".....once the carrier microbe is present in the animal, the antigen needs to become available to the animal's immune system. This may be accomplished when the carrier microbe dies so that the antigen molecules are released. ... In this way, it is possible to use a viable microbe that will persist in the vaccinated animal, for example, in the Peyer's patches and continue to produce antigen, thereby continually inducing antibody formation." (Emphasis added)

It is clear, therefore, that Gurtiss III contemplates only expression of antigen by the carrier avirulent microbe. The reference contemplates no production of antigen following death of the carrier microbe. Any antigen is produced only by the avirulent microbe, even after uptake by the Peyer's patches.

The Examiner asserts in the Final Action that:

> "Inherently the reference anticipates the instantly claimed invention because Salmonella-mediated delivery of a nucleic acid molecule encoding a Chlamydia antigen to the GALT elicits an immune response because the avirulent Salmonella mutants have lost the ability to cause disease without impairment in their ability to attach to and invade the GALT, and the instantly claimed invention has not been distinguished from the invention of Gurtiss III."

It is submitted, for the reasons discussed above with reference to disclosure of Gurtiss III, that the reference does not "inherently anticipate" the claimed invention. It is agreed that the avirulent Salmonella molecule have lost their ability to cause disease without impairment of their ability to invade the host. As discussed above, Gurtiss III, discloses that, following invasion of the Peyer's patches, the avirulent Salmonella releases the antigen it produces to the Peyer's Patches. There is no suggestion in Gurtiss III that the Peyer's patches themselves are producing antigen. It is only the Salmonella which produces antigen. As to distinction of the claimed invention over Gurtiss III, it is submitted that applicants claim language clearly distinguishes over the disclosure of Gurtiss III as discussed above:

> "An attenuated strain of an auxotrophic bacterium harbouring a vector comprising a nucleic acid molecule ... and a promoter operatively coupled to said nucleic acid molecule for expression of said *Chlamydia*

> protein or fragment thereof by cells of the host .....but not by said attenuated bacteria." (Emphasis added)

In Gurtiss III, the antigen is always produced by the attenuated bacteria.

As pointed out in response to the prior Office Action, the earliest date of filing of Gurtiss III (June 1987) predates any notion of DNA immunization to effect foreign gene expression by a host to which an expression vector is administered. It is believed that Ulmer et al (1993, ref. 39 herein) is the earliest paper contemplating DNA immunization.

In response to the prior Office Action, the applicants pointed to the discussion in the patent application with respect to the relevance of Gurtiss III and the apparent agreement of the Examiner thereto in allowing that application, which subsequently granted as US Patent No. 6,676,949. In the Final Action, the Examiner points to differences in the scope of the claims pending in this application and those of the granted US Patent, arguing that the traversal was not commensurate in scope with the instantly claimed invention. While not specifically agreeing with the Examiner's position, the applicants are content not to pursue this argument further at the present time.

In response to the prior Office Action, the applicants had stated:

> "It is the promoter in the DNA construct that directs expression of the MOMP in the host cells only and not in the attenuated bacteria."

The Examiner takes issue with this statement in the Final Action, stating that:

> ".... The *Salmonella* strains are considered to be carrier strains of attenuated bacteria for the expression of heterologous immunogen in a host cell, specifically the cells of the host GALT."

As discussed specifically above with respect to Gurtiss III, the *Salmonella* strains express the heterologous immunogen. While *Salmonella* are invasive bacteria, there is no contemplation whatsoever in Gurtiss that a vector harboured by the attenuated

Salmonella would enter into the animal host cells and that the host cells would express a *Chlamydia* antigen or fragment thereof. In this regard, the Examiner's attention is directed to the above quotation from Gurtiss, col. 10, ll. 10 to 24.

While the Examiner is correct that the *Salmonella* strains may enter host cells, such as GALT, it is the *Salmonella* strains which express the antigen to the invaded cells and not the invaded cells themselves. Again, the Examiner's attention is directed to col. 10, ll. 10 to 24.

Having regard to the above, it is submitted that the rejection of claims 19, 22, 25 and 27 to 28 under 35 USC 102(e) as being anticipated by Gurtiss III should be withdrawn.

Turning now to consideration of the rejection of claims 20 to 21, 24 and 26 under 35 USC 103(a) as being unpatentable over Gurtiss III in view of Brunham, the teachings of Gurtiss have been fully discussed above. Brunham describes a vector comprising a nucleic sequence encoding a MOMP or MOMP fragment and a promoter sequence operatively coupled to the mutated sequence for expression of the MOMP in a host and the production of an immune response to the MOMP upon administration of the vector to the host.

In the Final Action, the Examiner states:

> "It is the position of the Examiner that Brunham describes additional means for the expression of a Chlamydial antigen in a host cell, wherein Gurtiss III described an attenuated Salmonella typhimurium bacteria harbouring an expression vector that comprised a nucleic acid molecule encoding a Chlamydia antigen, wherein the attenuated carrier Salmonella strain expressed the nucleic acid gene product intracellularly for induction of an immune response and Brunham described a species of Chlamydia antigen coding sequence, specially the nucleic acid that encodes a MOMP protein from trachomatis under the control of a cytomegalovirus promoter placed in the plasmid vector is pcDNA3." (emphasis added)

First of all, the vector described by Brunham is intended for DNA immunization where the host cells express the MOMP and results in an immune response to the

MOMP. As has been extensively discussed above, the constructs described by Gurtiss are designed for expression of the antigen by the attenuated bacteria. Whether the attenuated bacteria invade host cells, the mechanism of expression remains the same and the antigen is expressed by the attenuated bacteria and not by the host cell. Since the vectors are fundamentally different in mechanism of operation, it follows that there is no motivation to utilize the vector of Brunham in the attenuated bacteria of Gurtiss III.

Accordingly, it is submitted that claims 20 to 21, 24 and 26 are patentable over the applied prior art and hence the rejection of claims 20 to 21, 24 and 26 under 35 USC 103(a) as being unpatentable over Gurtiss III in view of Brunham, should be withdrawn.

The Examiner rejected claim 19 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 8, 10, 15 and 17 of US Patent No. 6,872,814.

A rejection of obviousness-type double patenting may be overcome by the submission of a terminal disclaimer signed by an attorney of record. Submitted herewith is a Terminal Disclaimer, executed by an attorney of record, disclaiming the term of the patent to be granted on this application which may extend beyond the term of US Patent No. 6,872,814. Authorization to charge the prescribed fee to our deposit account is enclosed.

Having regard to the submission of the Terminal Disclaimer, it is submitted that claim 19 no longer is open to rejection under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 8, 10, 15 and 17 of US Patent No. 6,872,814 and hence the rejection should be withdrawn.

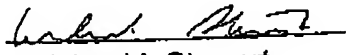
The patent numbers of pending applications which have now proceeded to grant have been added to pages 4 and 9.

Entry of this Amendment after Final Action is requested in that the application thereby is placed in condition for allowance. In the event the Examiner considers that the Amendment does not place the application in condition for allowance, the Amendment nevertheless should be entered, since the claims thereby are placed in better form of appeal and/or the issues for consideration on appeal are reduced thereof.

In the event the Examiner considers that further modification to the claim language is desirable to define the patentable subject matter thereof, the Examiner is requested to call the undersigned, Mr. Michael Stewart, collect, at the number given below, in order to arrive at mutually-acceptable language.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,



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